ORIGINAL ARTICLE

The Clinical Frailty Scale as a triage tool for ICU admission of dialysis patients with COVID-19: an ERACODA analysis

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GRAPHICAL ABSTRACT

The Clinical Frailty Scale as a triage tool for ICU admission of dialysis patients with COVID-19: an ERACODA analysis

Background
Several guidelines recommend using the Clinical Frailty Scale (CFS) for triage of critically ill COVID-19 patients. This study evaluates the impact of CFS on intensive care unit (ICU) admission rate, and hospital- and ICU mortality rates in hospitalized dialysis patients with COVID-19.
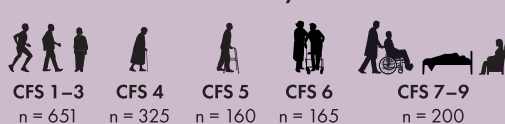
Methods
n = 1501
Hospitalized dialysis patients diagnosed with COVID-19
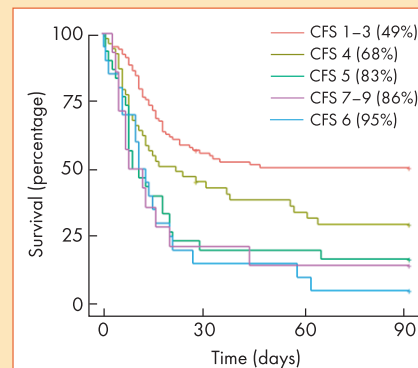
Clinical Frailty Scale
CFS 1–3 n = 651
CFS 4 n = 325
CFS 5 n = 160
CFS 6 n = 165
CFS 7–9 n = 200

Results
ICU admission rate
CFS 7–9 vs. CFS 1–3
OR 0.49
[0.27–0.89]

ICU 3 month survival rate
CFS 1–3 (49%)
CFS 4 (68%)
CFS 5 (83%)
CFS 7–9 (86%)
CFS 6 (95%)

Conclusion
Frail dialysis patients with COVID-19 were less frequently admitted to the ICU. Large differences in ICU mortality rates between fit and frail patients suggest that CFS may be a useful complementary triage tool for ICU admission in dialysis patients with COVID-19.

NEPHROLOGY DIALYSIS TRANSPLANTATION

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ABSTRACT

Background. Several guidelines recommend using the Clinical Frailty Scale (CFS) for triage of critically ill coronavirus disease 2019 (COVID-19) patients. This study evaluates the impact of CFS on intensive care unit (ICU) admission rate and hospital and ICU mortality rates in hospitalized dialysis patients with COVID-19.

Methods. We analysed data of dialysis patients diagnosed with COVID-19 from the European Renal Association COVID-19 Database. The primary outcome was ICU admission rate and secondary outcomes were hospital and ICU mortality until 3 months after COVID-19 diagnosis. Cox regression analyses were performed to assess associations between CFS and outcomes.

Results. A total of 1501 dialysis patients were hospitalized due to COVID-19, of whom 219 (15%) were admitted to an ICU. The ICU admission rate was lowest (5%) in patients >75 years of age with a CFS of 7–9 and highest (27%) in patients 65–75 years of age with a CFS of 5. A CFS of 7–9 was associated with a lower ICU admission rate than a CFS of 1–3 [relative risk 0.49 (95% confidence interval 0.27–0.87)]. Overall, mortality at 3 months was 34% in hospitalized patients, 65% in ICU-admitted patients and highest in patients >75 years of age with a CFS of 7–9 (69%). Only 9% of patients with a CFS ≥6 survived after ICU admission. After adjustment for age and sex, each CFS category ≥4 was associated with higher hospital and ICU mortality compared with a CFS of 1–3.

Conclusions. Frail dialysis patients with COVID-19 were less frequently admitted to the ICU. Large differences in mortality rates between fit and frail patients suggest that the CFS may be a useful complementary triage tool for ICU admission in dialysis patients with COVID-19.

Keywords: COVID-19, dialysis, frailty, intensive care units, mortality, triage

INTRODUCTION

Patients who are admitted to the hospital with coronavirus disease 2019 (COVID-19) can develop severe COVID-19, possibly necessitating intensive care unit (ICU) admission. Whether a particular critically ill patient will benefit from ICU admission in such circumstances is a question that is difficult to answer. In addition, limited ICU capacity can necessitate a selection of patients admitted to the ICU when there is an overwhelming demand for ICU beds during a pandemic. In these situations, physicians would be greatly supported by the development of guidelines on triage of specific high-risk patients with COVID-19.

Several national guidelines have recommended the use of frailty, in addition to well-known prognostic factors such as age and comorbidity, as a tool to triage patients for ICU admission [1–3]. To assess frailty, these guidelines use the Clinical Frailty Scale (CFS), which was originally designed and validated for assessment of frailty in patients >65 years of age [4]. In patients diagnosed with COVID-19, the CFS was also found to be useful to predict adverse health outcomes and mortality in the setting of the emergency department [5] and the hospital ward [6, 7]. In patients ≥65 years of age with serious comorbidities, the proposed cut-off values of the CFS for admission of COVID-19 patients to the ICU ranges from ≥5 to ≥6 [1, 3].

Dialysis patients are particularly at risk for a severe course of COVID-19 due to their older age and high prevalence of comorbidity. Dialysis treatment was associated with higher COVID-19-related mortality rates, reported to be 16–34% in dialysis patients in the first pandemic wave [8–12]. Age and frailty strongly affect mortality risk in dialysis patients both with and without COVID-19 [8, 13–17]. Previous data from the European Renal Association COVID-19 Database (ERACODA) demonstrated a steep increase in case fatality rates with increasing age and frailty in dialysis patients and kidney transplant recipients [8]. Moreover, older age, higher

frailty score and ICU admission were associated with a lower likelihood to reach pre-COVID-19 functional status in dialysis patients with COVID-19 [13]. To date, however, there are no data available on the use of CFS for the decision to admit dialysis patients with COVID-19 to the ICU. We therefore assessed the relationship between CFS at presentation and ICU admission rates as well as hospital and ICU mortality rates in dialysis patients hospitalized for COVID-19.

MATERIALS AND METHODS

Study population

The ERACODA was established in March 2020 and contains prospectively collected granular data on adult (≥18 years of age) dialysis patients or kidney transplant recipients who were diagnosed with COVID-19 [18]. The COVID-19 diagnosis was based on a positive result on a real-time polymerase chain reaction (PCR) assay or a rapid antigen test of nasal and/or pharyngeal swab specimens and/or compatible findings on a computed tomography scan or chest X-ray of the lungs. Data on patients were reported on a voluntary basis by physicians responsible for their care. For the current analysis, we included all dialysis patients admitted to the hospital with COVID-19 between 1 February 2020 and 1 May 2021 who had complete information on CFS and vital status at 3 months after first presentation.

Data collection

The ERACODA database is hosted at the University Medical Center Groningen (UMCG), Groningen, The Netherlands, and uses REDCap software (Research Electronic Data Capture, Vanderbilt University Medical Center, Nashville, TN, USA) to support data capture for research [19]. The study was assessed by the institutional review board of the UMCG. Because of the observational, non-interventional nature, the institutional review board deemed the collection and analysis of data exempt from ethics review regarding the Medical Research Involving Human Subjects Act.

Detailed information was collected on patient characteristics [demographics, frailty (referring to the clinical situation just before COVID-19), comorbidities, primary kidney disease, hospitalization, ICU admission and medication use] and COVID-19-related characteristics (presenting symptoms, vital signs and laboratory test results) at presentation. Age was categorized into three age categories: <65, 65–75 and >75 years. Frailty was assessed at presentation by using the CFS. The CFS categories range from 1 to 9, representing very fit to terminally ill patients, respectively [20]. For the current analysis, the CFS was categorized as fit to managing well (CFS 1–3), mild to moderate (CFS 4, 5 and 6) and severe (CFS 7–9). CFS categories 4–6 are presented separately because the cut off values for triage vary across countries.

Smoking status was scored as never, prior or current use. Comorbidities were recorded at presentation from the patient records and obesity was defined as a body mass index (BMI) >30 kg/m^2. Primary kidney disease was recorded according to the European Renal Association (ERA) coding [21]. Contributing countries were categorized into three different regions in an arbitrary manner based on geographical location. The following regions were chosen: northwestern Europe (Austria, Belgium, France, Germany, Luxembourg, The Netherlands, Switzerland, the UK, Sweden, Norway, Latvia and Finland), southern Europe including non-European countries around the Mediterranean Sea (Spain, Portugal, Slovenia, Italy, Albania, Bosnia and Herzegovina, Croatia, Greece, Serbia, Turkey, Syria, Morocco, Egypt and Libya) and eastern Europe (Czech Republic, Poland, Romania, Russia, Slovakia and Ukraine). Information on functional and mental health outcomes was collected by treating physicians at 3 months after the COVID-19 diagnosis. Since nephrologists generally meet their haemodialysis (HD) patients every week and know their patients well, we asked them to report whether the functional and mental status of their patients had fully recovered after 3 months (yes/no). Due to the study design, we had no options to invite individual patients to report on their functional and mental outcome.

Statistical analysis

Continuous data are presented as mean with standard deviation (SD) or as median with interquartile range (IQR) in case of a non-normal distribution. Categorical data are presented as absolute numbers and percentages. Baseline characteristics were compared between CFS categories using Student's t-test for continuous variables (Mann–Whitney U-test for non-normally distributed data) and Pearson chi-squared statistics for categorical variables.

The primary outcome was ICU admission and secondary outcomes were hospital and ICU mortality at 3 months after the first presentation. We used Cox regression analyses with a fixed follow-up time to estimate risk ratios (RRs) of ICU admission with 95% confidence intervals (CIs). A fixed follow-up time was used because the time of ICU admission greatly depends on the disease severity at presentation in the emergency department. Cox proportional hazards regression analysis was performed to estimate hazard ratios for the association between frailty and mortality at 3 months. To account for potential confounders, multiple models were constructed. In model 1 we adjusted for age and sex and in model 2 we additionally adjusted for BMI, smoking status (current/prior/never) and region (northwestern Europe, southern Europe, eastern Europe). In model 3, we additionally adjusted for comorbidities, including obesity, hypertension, diabetes mellitus, coronary artery disease, heart failure, chronic lung disease, active malignancy and autoimmune diseases. These analyses were performed in all hospitalized patients and in patients who were admitted to the ICU. Subsequently we stratified the relationship between CFS score and 3-month in-hospital mortality by age category (<65, 65–75 and ≥75 years). In addition, we repeated the analysis stratified by region. Finally, we use descriptive statistics to compare the recovery of functional and mental health status (yes/no) at 3 months after ICU admission categorized by CFS.

Missing data in the multivariable models were handled by multiple imputation (10 imputed datasets) with the chained

equations method using all variables included in the model [22]. All analyses were performed with Stata version 14 (StataCorp, College Station, TX, USA). A two-sided *P*-value of .05 was considered statistically significant.

RESULTS

On 1 May 2021, data on 4674 patients was collected in the ERACODA, including 3380 dialysis patients, of whom 1860 were hospitalized for COVID-19. After exclusion of patients with missing CFS data and/or lack of a 3-month follow-up, the study cohort consisted of 1501 patients (Supplementary data, Fig. S1). The treatment modality was HD in 94% of the patients and peritoneal dialysis (PD) in 6% of the patients, with an average (± SD) dialysis vintage of 5.2 ± 4.5 years (Table 1). The mean age was 68 ± 14 years, 63% were male and 81% of the patients were Caucasian. There were 651 patients with CFS 1–3 (43%), 325 patients with CFS 4 (22%), 160 patients with CFS 5 (11%), 165 patients with CFS 6 (11%) and 200 patients with CFS 7–9 (13%). Patients with CFS 1–3 were younger (61 ± 14 years); were less frequently diagnosed with diabetes (37%), coronary artery disease (24%) and heart failure (13%); and more frequently lived in eastern Europe than those with higher CFS scores. The CFS category was not associated with the duration of hospitalization.

As shown in Supplementary data, Table S1, hospitalized patients with missing CFS values more often had obesity (32% versus 22%), coronary artery disease (55% versus 34%) and heart failure (36% versus 25%) than patients with available CFS data.

ICU admission

Of the 1501 hospitalized dialysis patients, 219 (15%) were admitted to the ICU. The median time between hospital admission and ICU admission was 3 days (IQR 1–7) and did not differ between CFS categories (*P* = .4). The ICU admission rates ranged from 5% to 27% across different CFS and age categories (Table 2). The highest ICU admission rate was 27% in patients 65–75 years of age with CFS 5 and the lowest was 5% in patients >75 years of age with CFS 7–9. Multivariable analysis revealed that CFS 7–9 was associated with a lower rate of ICU admission compared with CFS 1–3 after adjustment for age and sex [7% versus 16%; RR 0.49 (95% CI 0.27–0.87), *P* = .02; Table 3]. Additional adjustment for BMI, smoking status, region and comorbidity did not change this result. Supplementary data, Table S2 shows the chance of ICU admission for the three European regions separately. In northwestern and southern Europe, the chance of being admitted to an ICU was lower in frail patients compared with patients with CFS 1–3. The opposite was true in eastern Europe, where a higher frailty score increased the chance of being admitted to an ICU.

Hospital mortality

After 3 months of follow-up, the mortality rate was 34% in the 1501 hospitalized patients and this rate rose with increasing age and CFS category, as shown in Fig. 1 and Supplementary data, Fig. S2. The highest mortality rate was 69% in patients >75 years of age with CFS 7–9, whereas the lowest mortality rate was 11% in patients <65 years of age with CFS 1–3 (Table 4). Multivariable analysis revealed that each of the CFS categories 4, 5, 6 and 7–9 were significantly associated with a higher hospital mortality rate compared with CFS 1–3 [CFS 4: RR 2.4 (95% CI 1.8–3.1), CFS 5: 3.3 (2.4–4.4), CFS 6: 3.6 (2.7–4.9), CFS 7–9: 4.9 (3.7–6.5); see Supplementary data, Table S3]. Additional adjustment for BMI, smoking status, region and comorbidity did not change the results. The association between CFS and 3-month mortality remained statistically significant across all age categories (Supplementary data, Table S4).

ICU mortality

The 3-month mortality rate in ICU-admitted patients was 65% (Supplementary data, Fig. S2). Only 3 of 34 patients (9%) with a CFS of 6–9 survived ICU admission, irrespective of age (Table 4). The lowest mortality rate was ∼50% in patients with CFS 1–3, with no clear difference between age groups. Multivariable analysis revealed that each of the CFS categories 4, 5, 6 and 7–9 were significantly associated with a higher ICU mortality rate compared with CFS 1–3 [CFS 4: RR 1.6 (95% CI 1.0–2.5), CFS 5: 2.4 (1.4–3.9), CFS 6: 2.8 (1.6–4.9), CFS 7–9: 2.7 (1.4–5.1); see Supplementary data, Table S3]. Adjustment for age and sex only led to a non-significant difference in ICU mortality for CFS 4 [RR 1.5 (95% CI 0.9–2.3)]. Additional adjustment for other confounders did not change the results.

Functional and mental health outcomes after ICU admission

Of the 219 ICU-admitted patients, 77 were still alive 3 months after ICU admission and data were available on functional and mental recovery for 52 of them (Supplementary data, Table S5). In 37 patients with CFS 1–3, recovery of functional status to a pre-existing level was observed in 70% of the patients, whereas mental status had recovered in 84% of the patients (Supplementary data, Table S5). Only six patients had a CFS ≥5, but all showed an almost complete recovery of functional and mental status.

DISCUSSION

This study demonstrates that during the first year of the COVID-19 pandemic, ICU admission rates were lower among the frailest hospitalized dialysis patients with COVID-19. In addition, hospital and ICU mortality rates were highest in these frailest dialysis patients when admitted for COVID-19. Of the ICU-admitted dialysis patients with CFS ≥5, more than 80% died within 3 months after ICU admission, irrespective of age. In contrast, fit to mildly frail dialysis patients with COVID-19 had a 40–55% survival rate when admitted to the ICU, with physician-reported functional and mental recovery at 3 months of follow-up. These findings suggest that the use

Table 1: Characteristics of hospitalized dialysis patients according to the CFS category.

Characteristics	All (N = 1501)	CFS 1–3 (n = 651)	CFS 4 (n = 325)	CFS 5 (n = 160)	CFS 6 (n = 165)	CFS 7–9 (n = 200)
Patient characteristics						
Age (years), mean (SD)	68 (14)	61 (14)	71 (11)	73 (11)	74 (10)	75 (11)
Sex (male), *n* (%)	946 (63)	432 (66)	203 (62)	89 (56)	106 (64)	116 (58)
BMI, mean (SD)	26.5 (5.4)	26.4 (5.2)	26.5 (5.0)	26.9 (5.3)	27.6 (6.5)	25.8 (5.6)
Race, *n* (%)						
Asian	48 (3)	24 (4)	8 (2)	5 (3)	2 (1)	127 (70)
Black	67 (5)	36 (6)	9 (3)	7 (4)	5 (3)	27 (15)
Caucasian	1210 (81)	481 (74)	276 (85)	139 (87)	148 (90)	14 (8)
Other	149 (10)	100 (15)	29 (9)	7 (4)	5 (3)	14 (8)
Unknown	27 (2)	10 (2)	3 (1)	2 (1)	5 (3)	127 (70)
Region, *n* (%)						
Northwestern Europe	482 (32)	134 (21)	114 (35)	64 (40)	72 (44)	38 (23)
Eastern Europe	337 (22)	186 (29)	88 (27)	30 (19)	19 (12)	162 (81)
Southern Europe, Middle East and Northern Africa	677 (45)	330 (51)	120 (37)	66 (41)	73 (44)	113 (57)
Unknown	5 (0)	1 (0)	3 (1)	–	1 (1)	70 (35)
Smoking status, *n* (%)						
Never	662 (57.2)	324 (61)	142 (57)	68 (52)	55 (49)	73 (54)
Former	366 (31.6)	147 (28)	75 (30)	47 (36)	47 (42)	50 (37)
Current	130 (11.2)	59 (11)	34 (14)	15 (12)	11 (10)	11 (8)
Reason for screening, *n* (%)						
Symptoms only	883 (64)	358 (59)	205 (68)	91 (63)	102 (67)	127 (70)
Symptoms and contact	262 (19)	126 (21)	59 (19)	27 (19)	23 (15)	27 (15)
Contact only	121 (9)	62 (10)	20 (7)	13 (9)	12 (8)	14 (8)
Routine screening	120 (9)	58 (10)	19 (6)	14 (10)	15 (10)	14 (8)
Comorbidities, *n* (%)						
Obesity	293 (22)	120 (20)	59 (21)	39 (28)	37 (28)	38 (23)
Hypertension	1240 (83)	550 (85)	268 (82)	126 (79)	134 (81)	162 (81)
Diabetes Mellitus	689 (46)	242 (37)	163 (50)	87 (54)	84 (51)	113 (57)
Coronary artery disease	515 (34)	157 (24)	146 (45)	73 (46)	69 (42)	70 (35)
Heart failure	377 (25)	86 (13)	100 (31)	52 (33)	59 (36)	80 (40)
Chronic lung disease	225 (15)	68 (10)	58 (18)	27 (17)	29 (18)	43 (22)
Active malignancy	103 (7)	29 (4)	27 ()8	9 (6)	23 (14)	15 (8)
Autoimmune disease	66 (4)	32 (5)	17 (5)	5 (3)	4 (2)	8 (4)
Primary kidney disease, *n* (%)						
Primary glomerulonephritis	138 (20)	132 (21)	31 (10)	23 (14)	18 (11)	16 (8)
Pyelonephritis	26 (2)	8 (1)	6 (2)	3 (2)	5 (3)	4 (2)
Interstitial nephritis	44 (3)	17 (3)	10 (3)	8 (5)	3 (2)	6 (3)
Hereditary kidney disease	92 (6)	57 (9)	20 (6)	3 (2)	8 (5)	4 (2)
Congenital diseases	24 (2)	14 (2)	4 (1)	–	4 (3)	2 (1)
Vascular diseases	269 (18)	100 (16)	73 (23)	25 (16)	31 (19)	40 (21)
Secondary glomerular disease	91 (6)	32 (5)	25 (8)	9 (6)	8 (5)	17 (9)
Diabetic kidney disease	481 (32)	190 (30)	110 (34)	57 (36)	55 (34)	69 (35)
Other	79 (5)	28 (4)	15 (5)	13 (8)	12 (8)	11 (6)
Unknown	155 (10)	66 (10)	29 (9)	18 (11)	16 (10)	26 (13)
Dialysis modality, *n* (%)						
HD	1404 (94)	601 (93)	306 (95)	154 (96)	153 (93)	190 (95)
PD	91 (6)	47 (7)	17 (5)	6 (4)	12 (7)	9 (5)
Dialysis vintage (years), mean (SD)	5.2 (4.5)	5.3 (4.7)	5.0 (3.9)	5.0 (4.0)	4.9 (4.0)	5.4 (5.1)
COVID-19-related characteristics						
Presenting symptoms, *n* (%)						
Sore throat (yes), *n* (%)	196 (14)	93 (15)	46 (15)	19 (13)	19 (13)	19 (10)
Cough	772 (52)	324 (50)	189 (59)	81 (51)	91 (56)	87 (45)
Shortness of breath	630 (42)	217 (33)	168 (52)	78 (49)	69 (42)	98 (50)
Fever	914 (61)	405 (62)	212 (65)	88 (56)	92 (57)	117 (59)
Headache	162 (11)	87 (14)	34 (11)	16 (11)	11 (7)	14 (8)
Nausea or vomiting	180 (12)	72 (11)	53 (17)	20 (13)	17 (11)	18 (9)
Diarrhoea	209 (14)	89 (14)	51 (16)	23 (15)	18 (11)	28 (15)
Myalgia or arthralgia	364 (26)	169 (27)	81 (26)	43 (28)	33 (21)	38 (21)
Vital signs						
Temperature (°C), mean (SD)	37.5 (1.0)	37.5 (1.0)	37.5 (1.0)	37.5 (1.0)	37.4 (1.0)	37.4 (1.0)
Respiration rate (/min), mean (SD)	19 (5)	18 (4)	19 (5)	20 (5)	19 (5)	21 (6)
O_2 saturation room air (%), mean (SD)	93 (6)	94 (6)	93 (5)	92 (6)	93 (6)	92 (5)
Systolic BP (mmHg), mean (SD)	135 (26)	137 (23)	136 (26)	136 (28)	132 (29)	130 (28)
Diastolic BP (mmHg), mean (SD)	74 (15)	77 (14)	73 (15)	73 (15)	70 (17)	68 (16)
Pulse rate (bpm), mean (SD)	83 (16)	83 (15)	84 (17)	84 (18)	82 (16)	84 (15)
Laboratory test results						
Lymphocytes (×1000/μl), median (IQR)	0.9 (0.6–1.3)	0.9 (0.6–1.4)	0.8 (0.5–1.2)	0.9 (0.6–1.3)	0.8 (0.6–1.2)	0.9 (0.6–1.3)
CRP (mg/l), median (IQR)	92 (42–212)	120 (33–430)	119 (40–429)	107 (46–359)	90 (36–215)	113 (44–333)

Numbers may not add up to the total because of missing values.

bpm, beats per minute; CRP, C-reactive protein.

Table 2: ICU admission rates in hospitalized dialysis patients with COVID-19.

CFS	All		<65 years		65–75 years		>75 years	
	Hospital, *n*	ICU, *n* (%)	Hospital, *n*	ICU, *n* (%)	Hospital, *n*	ICU, *n* (%)	Hospital, *n*	ICU, *n* (%)
1–3	651	102 (15)	380	65 (17)	154	25 (16)	117	12 (10)
4	325	53 (16)	85	14 (16)	110	28 (26)	130	11 (9)
5	160	30 (19)	34	6 (18)	48	13 (27)	78	11 (14)
6	165	20 (12)	28	3 (11)	49	5 (10)	88	12 (14)
7–9	200	14 (7)	32	5 (16)	55	3 (6)	113	6 (5)
Total	1501	219 (15)	559	93 (17)	416	74 (18)	526	52 (10)

Table 3: Multivariable analysis of ICU admission in hospitalized dialysis patients with COVID-19.

CFS	*n*	ICU, *n* (%)	Model 1[a]		Model 2[b]		Model 3	
			RR (95% CI)	*P*-value	RR (95% CI)	*P*-value	RR (95% CI)	*P*-value
1–3	651	102 (16)	Ref.		Ref.		Ref.	–
4	325	53 (16)	1.11 (0.78–1.58)	.6	1.09 (0.76–1.56)	.6	Ref.	.9
5	160	30 (19)	1.29 (0.84–1.99)	.2	1.30 (0.84–2.01)	.2	1.03 (0.72–1.49)	.4
6	165	20 (12)	0.84 (0.51–1.40)	.5	0.85 (0.51–1.42)	.5	1.21 (0.78–1.88)	.4
7–9	200	14 (7)	0.49 (0.27–0.87)	.02	0.52 (0.29–0.94)	.03	0.82 (0.49–1.37)	.02

[a] Adjusted for age and sex.
[b] Adjusted for age, sex, BMI, smoking status and region.
[c] Adjusted for age, sex, BMI, smoking status, region and comorbidity (obesity, hypertension, diabetes mellitus, coronary artery disease, heart failure, chronic lung disease, active malignancy and autoimmune diseases).
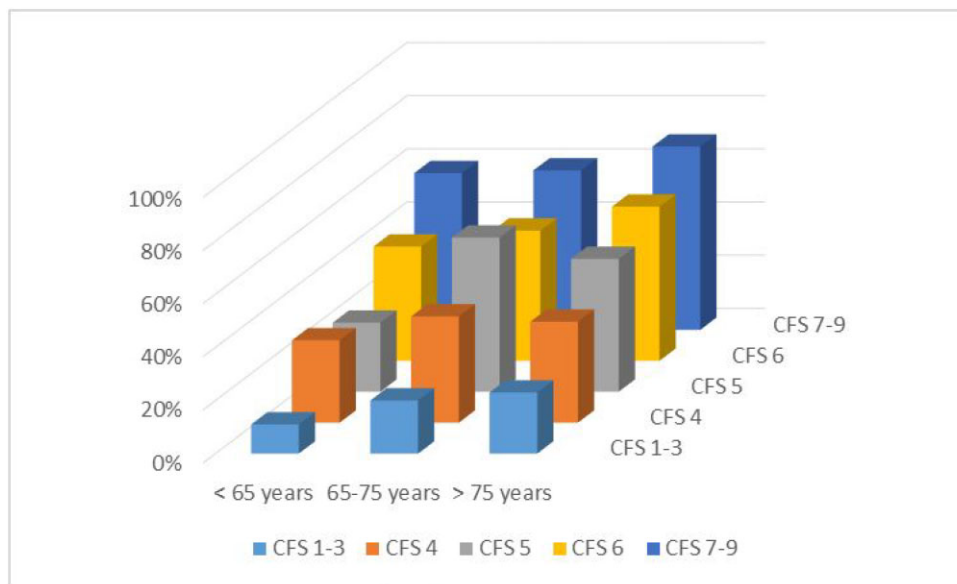

Figure 1: Three-month mortality of hospitalized patients per age and CFS categories.

of CFS can help clinicians to triage dialysis patients for ICU admission in cases of COVID-19.

The use of CFS for estimating a patient's prognosis in case of ICU admission has been studied mainly in patients >80 years of age. Both Flaatten *et al.* [15] and Guidet *et al.* [16] found a positive association between CFS and 30-day ICU mortality in patients >80 years of age without kidney disease. In addition, frailty has recently been associated with worse outcome during long-stay ICU admission [23]. The surge of COVID-19 during the first year of the pandemic caused a great need for available ICU capacity in many countries. The international consensus is that optimal patient care and allocation of ICU resources should be based on an estimation of the prognosis to survive

[24, 25]. This led to the implementation of guidelines for ICU triage of COVID-19 patients in which CFS was introduced as an instrument for triage. The proposed CFS cut-off values ranged from ≥5 to ≥6 in different guidelines [1, 3]. In response to the National Institute for Health and Care Excellence guideline recommendations, Darvall *et al.* [26] investigated the utility of CFS for triage in critically ill adults with non-COVID-19 pneumonia in Australia and New Zealand. Using a multicentre retrospective cohort design, they found that compared with lower frailty scores, severe frailty (CFS ≥7) was associated with increased ICU mortality. Although this patient group accounted for only 7% of the total ICU population, they recommended the use of CFS ≥7 as a threshold for excluding

Table 4: Hospital mortality (upper panel) and ICU mortality (lower panel) rates at the 3-month follow-up in dialysis patients with COVID-19.

CFS	All		<65 years		65–75 years		>75 years	
	n	Mortality, n (%)	n	Mortality, n (%)	n	Mortality, n (%)	n	Mortality, n (%)
Hospital mortality								
1–3	651	99 (15)	380	41 (11)	154	31 (20)	117	27 (23)
4	325	119 (37)	85	26 (31)	110	44 (40)	130	49 (37)
5	160	76 (48)	34	9 (27)	48	28 (58)	78	39 (50)
6	165	87 (53)	28	12 (43)	49	24 (49)	88	51 (58)
7–9	200	130 (65)	32	19 (59)	55	33 (60)	113	78 (69)
ICU mortality								
1–3	102	50 (49)	65	29 (45)	25	15 (60)	12	6 (50)
4	53	36 (68)	14	7 (50)	28	21 (75)	11	8 (73)
5	30	25 (83)	6	5 (83)	13	10 (77)	11	10 (91)
6	20	19 (95)	3	2 (67)	5	5 (100)	12	12 (100)

patients from ICU admission if triage was based on expected mortality. If the goal was to reduce the ICU occupancy, then a stricter CFS cut-off value of ≥ 4 was advised.

The use of CFS to predict hospital outcomes in patients with COVID-19 has been studied mainly in patients without kidney disease. In patients with suspected COVID-19, Simon *et al.* [5] found a higher risk of being admitted to the ICU when the CFS was ≥ 5 at presentation in the emergency department. In a large multicentre retrospective cohort study, Sablerolles *et al.* [7] found a higher risk of ICU admission in patients with CFS ≥ 6 in all age categories when compared with fit patients with CFS 1–3. In dialysis patients with COVID-19, highly varying ICU admission rates were reported. In their systematic review, Alfano *et al.* [27] report on ICU admission rates ranging from 2.6% to 70.5%. In our study, we observed a lower ICU admission rate in dialysis patients with CFS 7–9 compared with dialysis patients with CFS 1–3. In dialysis patients with CFS 4, 5 or 6, ICU admission rates were similar to those in patients with CFS 1–3. Since the use of CFS in triaging critically ill COVID-19 patients was already recommended early in the first pandemic waves by national guidelines in different countries across Europe, we presume that CFS was already applied in ICU triage of dialysis patients in our cohort, explaining the lower ICU admission rates in patients with CFS 7–9. Interestingly, we observed differences between European regions. While higher frailty was associated with a lower chance of being admitted to the ICU in northwestern and southern Europe, ICU admission rates were the lowest in patients with CFS 1–3 in eastern Europe. Differences in ICU admission rates might be explained by variations in COVID-19 healthcare policies, limited ICU capacity or cultural and religious interregional variations. Reasons for ICU admission were often not registered and therefore we cannot further explore our hypotheses for these interregional differences in ICU admission rates.

Dialysis patients were found to be at high risk for a severe course of COVID-19. Hospital mortality rates at 28 days ranged from 16% to 26% during the first year of the pandemic [8–12, 28, 29]. Nevertheless, associations between CFS and mortality have rarely been studied in dialysis patients, whereas in COVID-19 patients without kidney disease, this association has previously been observed [17]. A previous analysis of ERACODA data demonstrated a steep increase in case fatality

rates with increasing age and frailty in dialysis patients and kidney transplant recipients [8]. In addition, higher hospital and ICU mortality rates were observed in dialysis patients with higher frailty scores after adjustment for age and comorbidity. We showed that the survival chances of dialysis patients strongly decline in all age categories if frailty increased. This suggests that frailty assessed by CFS may also be useful in dialysis patients <65 years of age. However, the significance of frailty in younger patients differs from that of frailty in the elderly. The CFS has not been widely validated in patients <65 years of age [20]. In dialysis patients <65 years of age, it is therefore important to use the CFS with caution.

Besides mortality as an objective endpoint to determine a patient's prognosis, the functional or mental outcome after ICU admission due to COVID-19 is also of importance. It has been observed that older age, higher frailty score and ICU admission were associated with a lower likelihood to reach pre-COVID-19 functional status in dialysis patients with COVID-19 [13]. Although our present data represent a limited number of dialysis patients who survived ICU admission, 70–80% of those with low to mild frailty scores at hospital admission did show recovery of functional and mental status. This indicates that it was probably the right decision to admit these patients to the ICU.

A major strength of our study is the prospective data collection on frailty and clinical outcomes in a large cohort of dialysis patients with COVID-19 from the start of the pandemic. This resulted in a large dataset of patients with a wide representation of CFS scores and age categories. Because of the international collaboration, we were able to provide data from many predominantly European countries. This enabled correcting for region, taking into account the diverse cultural background and ethical considerations across the European continent. The observational design of our study also has its limitations. First, the study design is not suitable for making a recommendation whether a specific CFS cut-off value could be applied for ICU triage in critically ill dialysis patients with COVID-19, due to confounding by indication. This is a result of the guidelines in force at that time advocating the use of frailty in ICU triage, contributing to the observed association between frailty and lower ICU admission rates. Further studies are needed to validate the use of a certain CFS cut-off value in this population. Second,

the majority of patients were included before the start of vaccination campaigns in the different countries. This limits the generalizability of our findings to the actual situation in which a large proportion of dialysis patients have been vaccinated. However, the immune response to vaccination is weaker in dialysis patients than in healthy controls [30, 31]. Dialysis patients are therefore considered to remain at risk for a serious course of COVID-19 and in case of new sever acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants. The course of future COVID-19 in dialysis patients may vary depending on the SARS-CoV-2 variant responsible for infection, the vaccination status and the vaccination response. Third, data registration in the ERACODA took place on a voluntary base, resulting in differences in contributions by countries across Europe. For this reason, results might not be generalizable to each individual European country. Fourth, the number of PD patients in our cohort was too low to perform a valid comparison between outcomes in PD and HD patients. Ultimately we observed a selection bias caused by the exclusion of patients without data on CFS who had a higher prevalence of obesity, coronary artery disease and heart failure and who are prone to a more severe disease course. We expect this to have led to bias away from the null, which means a stronger association between frailty and health outcomes than we have observed.

In conclusion, the frailest dialysis patients hospitalized for COVID-19 were less often admitted to an ICU. Dialysis patients with moderate to serious frailty who were admitted to the ICU had a very high risk for mortality, irrespective of age. Outcomes were better for mildly frail dialysis patients who were admitted to the ICU. These findings suggest that use of the CFS can help clinicians to triage dialysis patients for ICU admission in case of COVID-19. Further research is required to establish whether use of the CFS can also be recommended for dialysis patients in other healthcare settings. It remains crucial to take into account the personal values of patients and relatives as well as the considerations for individual decision making for ICU triage in dialysis patients with COVID-19.

SUPPLEMENTARY DATA

Supplementary data are available at *ndt* online.

AUTHORS' CONTRIBUTIONS

P.B., L.B., P.V., M.N., R.T.G. and M.H.H. designed the study, drafted the article and performed data analysis. P.B., L.B., L.B.H., R.D., P.V., C.F.M.F., A.C., M.I., C.R., K.J.J., M.N., R.T.G. and M.H.H. contributed to the data collection, contributed important intellectual content during the interpretation of the results and manuscript drafting and agree to be personally accountable for the individual's own contributions.

DATA AVAILABILITY STATEMENT

Collaborators that entered data in the ERACODA remain owner of these data. Therefore the database cannot be disclosed to any third party without the prior written consent of all data providers, but the database will be made available to the editorial offices of medical journals when requested.

CONFLICT OF INTEREST STATEMENT

On behalf of all authors, the corresponding author states that there are no conflicts of interest.

The results presented in this article have not been published previously in whole or part, except in abstract format.

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